The following information was submitted on 12/31/2006:

Name & Sponsoring Organization

First Name: Sherry
Last Name: Ward
Institution: BioTred Solutions
Affiliation: Consulting/Contract Lab
Are you submitting comments on behalf of a sponsoring organization? No
If yes, please enter the name of the organization:

Comments and Questions

1. Do you have comments on the priority areas for the development and validation of alternative test methods listed above?

   Yes, first I would like to comment that I would prefer to comment on the ICCVAM 5-year plan after seeing a draft of the plan, and I hope that the narrowly selected areas provided here for comment will not be the stakeholders only opportunity to comment on your 5-year plan. I agree that all of the priority areas listed are important. Some of the toxicity tests have alternative methods in the pipeline, and others are less promising. Why were these tests selected for the list? Were certain criteria used to rank them? Factors that could be considered include: animal suffering from the test, numbers of tests or animals used annually for a test, regulatory/scientific need for a better test, degree of current progress toward an alternative for a type of test, etc. I see all of these factors as important, and dont see a consistent rationale in the list provided. There are many important areas for test method development and validation and all of the toxicity tests being used for testing chemicals, human and animal drug development, environmental testing, etc. should be considered and prioritized by whatever criteria the key stakeholders determine to be most important. There are many types of tests not listed that should be considered, such as the preclinical tests for drug development and toxicity assessment. For example, there has been significant industry investment in developing in vitro and computational methods for ADME, and these assessments have the potential to perform better than the animal tests. However, industry currently views having good preclinical non-animal screens as a competitive advantage and some of the methods are not made available to smaller pharma companies and biotechs. Public validation of some of these promising methods could greatly reduce animal use in drug development.

2. Considering available science and technology, what development, translation, and validation activities are most likely to have the greatest impacts within the next five years on refining, reducing, or replacing animal use?

   There is a significant need for: 1) test method developers and academic expert panel members to understand the regulatory applications and implications, 2) an understanding of the concept that the biological model (cells, tissue, etc.) and the test/endpoint are two separate entities that need to be conceived and co-developed to obtain useful in vitro methods. We need biologically-relevant test models that can replicate human mechanisms of toxicity and that can be used to measure at least some of the relevant endpoints of human toxicity in the tissue of interest. Any one model does not have to be/do everything, but it has to replicate the significant features/mechanisms of the endpoint that is being evaluated. The concept of test battery is to use an appropriate combination of biologically-relevant

models and relevant endpoints to obtain a result that compares to the human response. This brings up another important point - that the current ICCVAM validation criteria have not usefully defined how to validate a test battery, 3) computational models for many purposes including taking test battery data and producing a meaningful in vitro score. Simulation models could be used to reduce the numbers of labs and chemicals needed to validate a test method. In general, simplifying the validation process will be essential for progress, and 4) toxicology research that is being done in regulatory and other government labs needs to be made public, and once developed to a useful stage should be conducted collaboratively with industry to develop methods that are useful for regulatory needs. Research being done in industry also needs to be shared. All parties know that working together would produce results faster&.

3. What research and development activities hold the greatest promise in the long-term for refining, reducing, or replacing animal use?

   Employing bioinformatics and systems biology to develop an understanding of the spectrum of complexity of the organism of interest (human) from the molecular level (-omics) to the cellular level to the physiological/organ level to the whole organism.

4. What are appropriate measures for evaluating progress in enhancing the development and use of alternative test methods?

   I hope this question indicates that NICEATM is going to use the Balanced Scorecard approach for establishing and evaluating their performance in enhancing the development and use of alternative test methods. Metrics would include: # test methods evaluated; # test methods validated; providing other types of support (technical, educational, financial,&) to industry and agencies to help them develop and conduct validation studies of test methods; providing educational and/or scientific workshops for stakeholders; refining/simplifying validation criteria and developing computation/statistical methods for data evaluation; efforts toward international harmonization of criteria, processes, and validation and acceptance of new methods; working with regulatory agencies to promote acceptance of methods